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Placentophagy: Therapeutic Miracle or Myth?

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INTRODUCTION

Postpartum women are consuming their placentas (placentophagy) encapsulated, cooked, and raw for the prevention of postpartum depression (PPD) and other perceived health benefits. Although almost all non-human placental mammals ingest their placentae at parturition, the first documented accounts of postpartum women practicing placentophagy were in North America in the 1970's (Ober 1979). In recent years, advocates and the media have popularized health benefits of the practice and more women are considering it as an option for postpartum recovery. Health care advocates claim that hormones and nutrients, including estrogen, progesterone, lactogen, iron, β-endorphins, and oxytocin, are retained through preparation and consumption (Apari and Rozsa 2006; Beacock 2012; Selander et al. 2013). Although the presence of some of these components, including progesterone (Piasek et al., 2001), iron (Bradley et al., 2004), and oxytocin (Sugahara et al., 1985), have been shown in term placenta, their maintenance and stability in raw tissue and in preparation, as well their effects after consumption on the postpartum woman have not been tested. Reported benefits of placentophagy include prevention of PPD, pain reduction, and increased milk production and energy. Other benefits proposed are the reduction of postpartum bleeding, more rapid uterine recovery, enhanced maternal bonding, and boosting of the immune system (http://www.PlacentaBenefits.info; http://www.Placentawise.com). Dehydrated and encapsulated placenta pills are encouraged for future consumption for treating insomnia and other sleep disorders, inflammation and scars, signs of aging in the skin and hair, and hormone regulation related to difficulties during menstruation and menopause.

Despite the many claimed benefits of placentophagy, it is unclear whether consumption of the placenta is advantageous. The placenta is not sterile (Aagard et al., 2014) and one function of the placenta is to protect the fetus from harmful exposure to substances. As a consequence, elements including selenium, cadmium, mercury, and lead, as well as bacteria

have been identified in post-term placental tissues (Aagaard et al., 2014; Iyengar and Rapp, 2001; Llanos and Ronco, 2009; Myllynen et al., 2005; Osman et al., 2000). Due to in utero or post-birth contamination bacteria or viruses may remain within post-term placental tissues. The potential adverse effects of these components of the placenta on the postpartum consumer and nursing infant are unknown.

Websites describe instructions for placental preparation that have not been standardized for efficacy or safety (e.g. www.placentawise.com). The placenta may be ingested raw, cooked, or dehydrated (raw or steamed) and encapsulated into pills for use over time. The method of preparation varies depending on the service provider and woman's motivation for treatment. Some providers adhere to Occupational Safety and Health Administration (OSHA) regulations for the safety and handling of placental tissue (e.g. http:// www.PlacentaBenefits.info), but these regulations do not include evidence of the therapeutic efficacy of consumption. Other websites provide "do it yourself" instructions with an array of preparation methods including baking placental tissue until "dry and crumbly" and placing it in a coffee grinder or food processer prior to encapsulating (http://healthyself.ning.com/profiles/blogs/placental-encapsulation). Health care advocates often cite the Compendium of Materia Medica, a comprehensive medical text of Traditional Chinese Medicine from the 16th century (Szhizhen and Xiwen 1593), as evidence of the long history of postpartum practice and the placenta's medicinal properties. Although Zi He Che, the Chinese term for dried human placenta, has historically been used for treating various ailments (e.g., impotence, liver and kidney problems, infertility, and low energy) in nonpostpartum humans, there is no clear evidence of postpartum women ingesting placenta (Young and Benyshek 2010). Evidence of efficacy of placentophagy or treatment for other ailments has not been demonstrated.

Despite the amount of information available to the public on the therapeutic benefits of placentophagy, there is no scientific evidence examining its effects in humans, and the data from animals are inconclusive. This review is designed to synthesize the published data on: 1) women's current attitudes, motivations, and experiences with maternal placentophagy; 2) empirical studies of human or animal consumption of human placenta, and 3) animal placentophagy studies selected based on relevance to human practice, with recommendations for additional research. The health benefits and risks of placentophagy warrant further investigation of the retained contents of the raw, cooked, and encapsulated placenta. The impact of placenta consumption on the postpartum woman and nursing infant remains to be elucidated, and health care professionals should be aware of the literature to support patients in their decision-making.

METHODS

A computerized search was conducted using PubMed, Medline Ovid, and PsychINFO for the period between January 1950 and January 2014. Key words included placentophagy, placentophagia, maternal placentophagia, maternal placentophagy, human placentophagia, and human placentophagy. After removing duplicates, a total of 49 articles were found. An attempt was made to identify and systematically review articles focused specifically on human placentophagy. Peer reviewed empirical studies of human attitudes, motivations, and

experiences with placentophagy (n=3) were included. However, with no peer reviewed empirical studies of effects of human placentophagy found in the initial search, articles that studied animal placentophagy were also included (n=1, review; n=3, empirical) based on relevance to human practice. Relevance in animal studies was determined if they 1) investigated animal consumption of human placenta or 2) authors discussed implications of empirical findings for human practice. Editorial commentaries were excluded. A total of 7 studies from the original search were included in this review.

Articles chosen (n = 7) were cross-referenced for articles not identified in the initial search. Empirical studies of human (n = 1) and animal (n = 1) consumption of human placenta were included as a result of the cross-reference. A total of one additional empirical animal study was chosen due to the author's discussion of benefits of placentophagy for facilitating labor in humans. A total of 10 articles (four human, six animal) were included in this review.

RESULTS

Placentophagy: Motivations, experiences, and attitudes

To investigate general knowledge and attitudes about placentophagy, Cremers and Low (2014) recruited male and female participants (N = 216; 18–22 yrs) from college email lists at a small liberal arts college in New England to complete online surveys. A majority (66%) reported some awareness of placentophagy (either human or animal) and a marginal but none significant difference (p < .06) was found based on gender, with women being slightly more familiar. No significant differences were found based on ethnicity (p = .21). Participants reported learning about the practice through various sources, including the media, a friend, education, or by observing it in animals. Only a small number (2.3%) reported that they had heard about placentophagy by medical professionals. Relatively few participants in this sample reported they had eaten cooked placenta (6 female, 1 male), and one had ingested raw tissue. The perceived benefits of consumption were not reported. Most respondents indicated that motivations for ingesting placenta were for non-specific nutritional or medicinal benefits, or because a midwife had suggested it. About a quarter of respondents (26.8%) reported they would consider placentophagy in the future for its perceived health benefits, including the prevention of postpartum depression. There were no significant differences based on gender (p = .45) or ethnicity (p = .16) in willingness to eat placental tissue.

Selander and colleagues (2013) published results of an Internet-based survey on the motivations and experiences of 189 women (91% from the United States and 7% from Canada) who had engaged in placentophagy. The majority of respondents were Caucasian (93%) with a median income of \$50,000 per year. Among the 189 women, 304 responses were provided for motivations for placentophagy. Almost half of the 189 participants (49%) reported a previous postnatal mood disorder, most frequently depression (47%) followed by the "baby blues" (24%) and anxiety (19%). The majority (63%) of the respondents stated that their mood disorder was self-diagnosed, however the authors did not distinguish which disorders were diagnosed by a professional versus self-diagnosed. Approximately half (52%) rated the severity of their mood disorder as "mild" and 43% described it as "severe." A small minority of respondents rated their disorder as "very severe" (3%) or "very mild"

(2%). The most frequent response for choosing placentophagy was to improve mood (n = 103; 34%). The most frequent health benefit reported after consumption was also improved mood (40% of total responses), followed by increased energy (26%) and improved lactation (15%). The majority of the sample considered placentophagy a positive overall experience, and 98% of the women reported they would engage in placentophagy again. The authors did not report whether placentophagy was preferred over other established treatments. The strong support in this study of perceived benefits of placentophagy is limited by the principal investigator's role as the founder of a placenta encapsulation service organization (http://www.Placentabenefits.info). Moreover, a relatively homogenous sample, potential biases in recruitment and no placebo comparator limit the validity of the findings.

Anthropological evidence of consumption, handling practices, and cultural beliefs about placenta

Young and Benyshek (2010) conducted an ethnographic systematic search of 179 societies in the electronic Human Relations Area Files in an investigation of cross-cultural placental beliefs and practices. Of the 179 societies, no references to maternal placentophagy (a woman's ingestion of her placenta post-birth) as part of cultural tradition, and only three references to non-maternal placentophagy for ritualistic or medicinal purposes, were found. One isolated account found of a postpartum mother, identified as Mexican/American, and her family ingesting the placenta was concluded not to be representative of any cultural tradition. A majority of societies were found to have culturally prescribed beliefs and methods for the handling of the placenta. For instance, many societies believe that burying the placenta in a specified location will ensure positive health outcomes for families and communities. Relatively few societies (n = 5) in a range of regions within Asia, Central America/Caribbean, South America, Africa, Middle East, endorsed the belief that the placenta has efficacy for treating physical or medical conditions, including infertility, cracked feet, and the prevention of baldness. The placenta was thought to be unclean, polluted or contagious among 12 societies. The authors concluded that there was no anthropological evidence to support the notion that human placentophagy is common practice. The authors suggest that its absence across cultures may be associated with limited observations by anthropologists, underreporting of participants, or a result of culturally learned knowledge that placental consumption is harmful (Young and Benyshek 2012).

Human Study: Effects of human placentophagy on milk production

Advocates of maternal placentophagy claim that placentophagy improves lactation. One dated study (Soyková-Pachnerová et al. 1954) investigated the physiological effects of placentophagy on milk production in humans. Of the 210 participants fed freeze-dried human placentas, 86% reported "good" (operationally defined as an increase of at least 20g in milk production) or "very good" (at least an increase of 30g) increases in milk secretion. The authors did not clarify whether mothers ingested their own placental tissue or that from donor placentas. There were no control groups in this study, although a subsequent non-controlled study found that 7 of 21 women fed disguised, freeze-dried beef had a "positive" increase in milk production compared to 14 of the 21 women with no increase in milk production after ingesting beef. Criteria for a "positive" increase were not described in the second study. Overall, these studies do not adhere to current scientific standards and

conclusions cannot be drawn. There was no set of inclusion criteria for participant selection, timing of entry into the study relative to birth and timing of placental consumption. Numerous other confounding factors (i.e. natural variations in the development of milk production within days after giving birth, whether mothers were taking medications, placebo effects, effects of participating in a study) were not controlled. It is also important to note that no other studies investigating the effects of placentophagy on lactation in humans were found in our literature search.

Animal studies: POEF and analgesic effects of placentophagy

Most empirical evidence of the therapeutic efficacy of placentophagy is derived from animal research. Kristal et al's work over the last 40 years (for review see Kristal et al. 2012) displays the most scientific and methodological rigor to explain a possible adaptive significance of placentophagy in non-human mammals for reducing pain during labor. In the review of a series of controlled experimental studies using rodents, Kristal and colleagues (2012) showed that placentophagy enhances endogenous opioid - or opiate - mediated analgesia. The authors suggest that analgesic effects are elicited in the woman's system through ingestion of a substance in the placenta and amniotic fluid called Placenta Opioid Enhancing Factor (POEF). The molecular composition of POEF has not been identified, but Kristal et al. suggest that, its action appears to be dependent on the preparation, dose, and timing of ingestion relative to giving birth and on the presence of elevated endogenous opioids in the woman's system. For example, in unpublished data discussed in Kristal et al.'s review, the authors reported that beneficial effects of POEF were preserved for months if the afterbirth material was frozen at -20° C (a temperature below that of most household freezers). However, the beneficial effects diminished after 24 hours at room temperature. Frozen tissue required heating between 35°C to 40°C to be effective, but lost its effects at higher temperatures. Analgesic effects were also only found when the dosage of afterbirth material was the equivalent of that coming from a single pup (Kristal, Abbott, & Thompson, 1988) and POEF effects were shown within five minutes of ingestion and lasting for approximately 40 minutes. Importantly, Kristal et al. found that ingestion of afterbirth in the absence of elevated opioids or opiates in the system, did not produce a change in pain thresholds. Based on these findings, the authors suggested that placentophagy may function to reduce pain during labor because this is the time when mammals have the placenta (and amniotic fluid) available and endogenous opioids are elevated. Since placental tissues are not available to humans until after the child is born and no studies were found that systematically studied placental consumption in conjunction with opiate-intake in humans, the relevance of these findings to reducing pain in labor or postpartum in humans is unclear.

Abbott and colleagues (1991) conducted a series of studies investigating the generalizability and specificity of mechanisms of action of POEF on enhancing analgesia in rodents. To evaluate the generalizability of effects of POEF, the authors investigated effects of human and dolphin placental ingestion on pain thresholds in female rats experiencing partially opioid-mediated analgesia produced by vaginal-cervical stimulation. Vaginal-cervical stimulation (i.e. probing) is a standardized laboratory procedure that has been shown to produce opioid mediated analgesia, thereby mimicking biochemical events at parturition. Sucrose was used as a control substance and substances were administered through an

orogastric tube. Rats given human and dolphin placenta showed a significantly greater increase in pain thresholds from pre-infusion to post-infusion compared to rats given sucrose. The authors concluded that POEF is contained in human and dolphin placentae. Notably, only one human placenta was tested in this study and, to our knowledge, the analgesic effects of human placental consumption have not been replicated in other rodent studies or in humans. Abbott and colleagues also investigated whether the opioid-mediated analgesic effects of POEF were found in male rats following placental consumption. Male rats fed donor rat placentas after morphine injections had significantly more elevation and prolongation of analgesia compared to male rats given morphine alone, morphine and beef, or saline controls.

In another study in this series, Abbott and colleagues (1991) did not find POEF to be contained in rat liver tissue and concluded that POEF is localized to placental tissue. Rats were fed pregnant-rat liver, beef or no meat, after injections of morphine and compared to rats given saline. As expected, morphine injection elevated the pain threshold compared to saline injection. However, no significant differences in pain thresholds were found in the experimental groups. When comparing effects of different administration locations (enteral, intraperitoneal, subcutaneous), enhancement of opioid-mediated analgesia occurred only when afterbirth was administered through the gastrointestinal tract (Abbott et al. 1991). Based on these findings, the authors suggested that the enhancing effect of POEF is localized to placental tissue and associated with biochemical events in the gastrointestinal system.

DiPirro and Kristal (2004) investigated the effects of POEF on central nervous system (CNS) opioid receptors to better understand endogenous mechanisms that are modified by placentophagy. Hotplate assays, tests of pain response in animals caused by heat to measure pain thresholds, and receptor-selective agonists were administered to virgin rats ingesting rat placentas or a control substance. Placenta ingestion was shown to potentiate δ -opioid and κ -opioid activity and enhance pain thresholds, and to attenuate μ -opioid activity. Conversely, a side effect of morphine when used in isolation has been shown to potentiate μ -opioid receptor activity (Sora et al. 1997; Mann et al. 1991), which is associated with the slowing of behavior and motor activity.

Another side effect commonly produced by opiates is the slowing of gut transit (i.e. constipation). Corpening and colleagues (2004) showed that ingested placenta reversed the slowing of gut transit in rodents. Rats that ingested placenta were found to have a reversal of the slowing of gut transit that was produced by morphine compared to rats that ingested liver. The authors conclude that ingestion of placenta (or amniotic fluid) by rats at parturition may help restore the digestive system after delivery.

Overall, the evidence on analgesic effects of placentophagy in rodents suggests a possible adaptive significance of placentophagy in nonhuman mammals during labor for increasing pain thresholds without inhibiting the ability to care for offspring (Kristal 2012). Furthermore, Kristal (1991) argued that the ingestion of amniotic fluid may be more relevant for enhancing pain thresholds than the placenta because mammals have access to it prior to delivery, when endogenous opioids are activated and pain relief is most needed. Health care

advocates assert that placentophagy helps to reduce pain over time and enhance maternal bonding (e.g. http://Placentawise.com). The current evidence from rodent studies, which found that beneficial effects were dependent on the dose and timing of ingestion suggests that mothers who ingest small amounts of the placenta hours and days postpartum may not experience an analgesic benefit. Currently, there are no controlled studies of the effects of POEF through placental consumption in humans.

Animal Study: Effects of placentophagy on prolactin, progesterone, and oxytocic activity

A study by Blank and Friesen (1980) exploring placental consumption in rats is commonly cited as evidence supporting the beneficial effects of maternal placentophagy for increasing lactation and regulating hormones postbirth (e.g. http://placentabenefits.info). Increased levels of prolactin and low levels of progesterone are associated with lactation. In their study, Blank and Friesen sought to quantify the physiological effects of ingested placenta on serum prolactin and progesterone concentrations in rats. Female rats that were allowed to ingest their placentas normally were found to have early elevations of serum prolactin levels (at day 1 postpartum) coupled with decreases in serum progesterone (on days 6 and 8 postpartum), compared to rats that were prevented from eating their placentas. Further, they found that the addition of 4g/day of rat placenta to the standard chow of rats treated with pregnant mare serum gonadotropin resulted in a similar and earlier decrease in progesterone levels at day 5. The authors argue that this apparent early rise in prolactin and decrease in progesterone may be important for facilitating a return to a normal cyclic estrogen cycle and promoting lactation.

Conclusions drawn from the data presented in the Blank and Friesen study (1980) are limited by several issues. First, while the rats that were allowed to eat their placentas had higher prolactin levels on day 1, this was the only time point studied for which a difference was found. There were no differences in the levels of prolactin in either group of rats at 2 hours, 2, 4, 6, or 8 days postpartum. Further, while the rats that ate their placentas did have lower progesterone levels at postpartum days 6 and 8, the concentrations of progesterone otherwise increased to a similar degree in both groups during the course of this study (approx. 7 fold increase in the group that ate placenta vs. approximate 9 fold increase in the group that did not eat placentas). The authors also observed contrasting results in their study. While the equivalent of 4g/day of placental extract resulted in decreased progesterone, it had no significant effects on prolactin levels. On the other hand, rats fed the equivalent of 2g/day of placental extracts had elevated, instead of depressed, progesterone levels at day 5. Finally, since the authors did not follow the rats in this study over time, it is not possible to know whether these relatively small changes in prolactin or progesterone early postpartum had any long - term effects or benefits. Blank and Friesen also found that rat consumption of human and bovine placenta extracts had no effect on prolactin and progesterone levels.

Animal Study: Effects of placentophagy on oxytocic activity

In a traditional obstetric practice in Nigeria, Onuaguluchi and Ghasi (1996) observed practitioners giving dried sheep placenta to women to induce labor. To investigate the presence of oxytocic activity in facilitating uterine contractions in sheep placental tissue, the effects of dried sheep placenta on multiple tissues from different species (guinea pig, rat,

cat) were tested. The authors found that dried sheep placentas had an "oxytocic" effect on isolated guinea pig uteri. Interestingly, boiling, autoclaving and high pH did not diminish this effect. The authors suggested that this "oxytocic" effect was the reason that ingesting dried sheep placenta could be used to facilitate labor in humans. However, while dried sheep placenta did induce uterine contractions in ex vivo guinea pig uteri, the potency was at least 1.6×10^6 (that is 1.6 million) times less effective than oxytocin itself, and 1×10^4 times less potent than histamine. In addition, while high pH had little effect on the activity of the dried sheep placenta, low pH resulted in a significant loss of effect. Taken together, this would suggest that the dose of dried placenta needed to achieve any meaningful effects would have to be extremely high, and that swallowing the dried placenta would essentially eliminate any potential effects it may have, due to the low pH environment of the human stomach.

DISCUSSION

Preliminary findings on women's perceptions and experiences suggest that women choosing placentophagy perceive multiple postpartum health benefits. A majority of respondents reported learning about placentophagy and its benefits through the media, acquaintances, or recommendations of midwives. Initial data of those choosing placentophagy include predominantly proponents of placentophagy, which is likely to positively skew results. More research is needed to determine whether benefits can be replicated in other populations with sound research methodology.

Kristal and colleagues (Abbott et al., 1991; Corpening et al., 2004; DiPirro & Kristal, 2004, Kristal et al., 2012) provided evidence that placentophagy (including placental and amniotic fluid ingestion) may function to enhance opioid-mediated analgesia during labor and delivery in rats, and enable adaptive maternal behavior (i.e. defined as contact and licking of pups). The authors suggested that their findings do not provide evidence in support of benefits of human placentophagy, but rather, that if the molecular composition of POEF is identified and isolated, it may aid in the development of adjunct pharmacological treatments for pain that serve to enhance pain relief without producing the negative side effects of opiates (e.g. constipation, disrupted maternal behavior). Current evidence indicates that analgesic effects of placentophagy in rodents at parturition are confined to specific parameters for the dosage, preparation, and timing of ingestion, including the presence of endogenous opioids or opiates in the rodent's system, (Kristal et al. 1988; Kristal 2012) that are not reflected in human placentophagy practice.

Proponents of placentophagy suggest that a primary motivation for engaging in placentophagy is to reduce or prevent PPD by replenishing hormones and nutrients that were lost during childbirth (Selander et al. 2013). Although PPD is understood to be partially precipitated by sensitivity to significant estrogen withdrawal post-delivery (Ahokas et al. 2001; Bloch et al., 2000; Gregoire et al. 1996; Okun et al. 2011; Wisner and Stowe 1997), current evidence does not suggest that placentophagy prevents or treats PPD by replenishing therapeutic doses of estrogen nor that it facilitates a return to a normal postpartum estrogen cycle. While it is clear that estrogen is significantly depleted at childbirth, not all women experience postnatal mood symptoms, thus the exact role of estrogen in PPD is not fully understood. Multiple psychosocial risk factors and biochemical events are attributed to the

onset and maintenance of PPD (Banker et al. 2014; Beck et al. 2001; Bloch et al 2003) and many of these factors are either not tested or not present in animal models, which makes animal data difficult to translate to human patients.

Animal data also do not support claims that placentophagy in humans helps to enhance lactation, reduce pain, facilitate uterine contraction, or replenish hormones (i.e. prolactin, estrogen, progesterone, oxytocin) associated with postpartum recovery since statistically significant findings in animal data do not translate into meaningful benefits for humans. Additionally, the placebo effect, which is very powerful in humans (Annoni 2013; Benedetti et al. 2011; Geers et al. 2013; Kirsch et al. 2014), is not tested in animal models. Reports of human benefit may, at least partially, be a result of placebo effects, which could be addressed through a randomized placebo-controlled clinical trial. Overall, human data on placentophagy enhancing milk production is dated, inconclusive and, to our knowledge has not been systematically investigated further. Based on the studies reviewed, it is not possible to draw any conclusions relevant to human health. We conclude that the animal and human data strongly support the need for more precise evaluation of the benefit, if any, of placentophagy practices in human patients.

Future studies need to investigate: 1) substances in raw placental tissue and their the stability and maintenance through the various preparations for consumption, 2) the effects of placentophagy on human health conditions, 3) whether perinatal events or post-birth handling has differential effects on the health of placental tissue and 4) changes in depressive and other symptoms using valid and reliable measures.

The authors of this paper are currently gathering data on the perceptions, beliefs, and placental practices of health care providers internationally and nationally, as well as patients locally, and whether providers are recommending placentophagy to patients. Preliminary findings in this study (n = 132) suggest that among national and international psychologists, psychiatrist, nurses, social workers, and medical residents who completed an internet survey, a small minority (4%) recommend placentophagy as a supplement over vitamins and iron supplements for non-specific postpartum health benefits and none recommended placentophagy as a treatment over antidepressant medications. Among patients, a relatively large percentage (29.5 %) who responded to a general question about their preference for placentophagy versus prescribed medications indicated that they were as equally willing to try placentophagy as they were willing to try prescribed medications. Also, 5% of patients reported that they were more willing to try placentophagy in place of prescribed medications without specification for any specific illness. Approximately 5% of respondents reported discussing placentophagy with health care providers. Further information on human practice as well as studies assessing efficacy and risk in humans are needed to determine whether there are beneficial or detrimental effects of placentophagy for assisting with labor and delivery, pain, or for other potential therapeutic applications.

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